REMARKS

Claims 1-11 were originally filed and were subject to a Restriction Requirement. Applicants affirm election, with traverse, of original claims 1-8 and 11, corresponding to the invention of Group I, and further to the species of SEQ ID NO:4 and its encoded polypeptide of SEQ ID NO:6 of that group, again with traverse. Applicants submit that the invention encompassed by claims 1-8 and 1 of Group I, drawn to SEQ ID NOs:4 and 6, could be examined together with claims 1, 2 and 10 of Group II drawn to a second product, a hybridization probe, without undue burden. Claim 1 recites no such "second product", and claim 2 has been amended to delete element c) reciting a "probe which hybridizes---". Thus claims 1-8 and 10-11 are coextensive and could be examined together without undue burden. Applicants further submit that the five polynucleotide sequences recited in claim 2, SEQ ID NO:1-5, are sufficiently few in number to not constitute an undue burden to be searched together. Finally, applicants submit that new claims 12-15, drawn to a combination comprising SEQ ID NO:1-5 and their use in microarray analysis, could also be examined together with the elected claims without further burden, considering that the finding of a single patentable sequence, e.g., SEQ ID NO:4, would render any combination containing that sequence patentable as well. Applicants therefore request reconsideration of the Restriction Requirement and examination of all sequences, SEQ ID NO:1-6 in claims 1-8 and 10-11 as well as new claims 12-15. In the event that the Examiner maintains the Restriction Requirement, Applicants reserve the right to pursue non-elected claims in subsequent divisional applications.

Justification for the amendments is as follows. The claims were amended to clarify the invention. Claim 1 has been canceled and claim 2 amended to independent form. Claim 2 has been amended at step (c) to recite "completely complementary", and at step (d) to delete reference to "a probe" and to recite "a naturally-occurring variant of (a), (b), or (c) having at least 95% identity to the polynucleotide sequence of (a), (b), or (c)". Likewise claim 3 has been canceled and claim 4 amended to independent form, and to recite an additional element (d) reciting "a variant of the polypeptide sequence of SEQ ID NO:6 having at least 95% identity to the polypeptide sequence of SEQ ID NO:6". Claims 7 and 8 have been amended to delete the term "pharmaceutical" from the phrase "pharmaceutical composition". Support for the amendment to claim 2 is found in the specification, for

example, at p.3, lines 27-33, and at p. 12, lines 18-22. Support for the amendment to claim 4 is found in the specification, for example, at p. 3, lines 27-33. New claims 12-15 have been added to claim the combination of polynucleotides, SEQ ID NO:1-5, and methods of use in microarray analysis. Support for new claims 12-15 are found throughout the specification, for example, for new claims 12 and 14, at p. 8, lines 3-4 (SEQ ID NO:1-5), and at p. 13, lines 29-33 (microarray analysis); for new claim 13, at p. 12, lines 29-32 (labeling moieties); and for new claim 15, at p. 7, lines 31-32 (diagnosis of neurotransmitter diseases). No new matter is added by any of these amendments, and entry of the amendments is therefore requested.

35 U.S.C. § 101, Rejection of Claims 1-8 and 11

The Examiner has rejected claims 1-8 and 11 under 35 U.S.C. § 101, because the claimed invention lacks patentable utility. The Examiner stated that while it is agreed that SEQ ID NO:6 encodes a polypeptide expressed by human nerve cells contemporaneous with the expression by these cells of neurotransmitter-processing enzymes, the specification and the prior art of record are silent as to the in vivo function of the polypeptide of SEQ ID NO:6, and no specific in vitro utility for SEQ ID NO:6 or the nucleic acid encoding SEQ ID NO:6, are disclosed.

The Examiner stated that whether a gene or its product have any role at all in regulation of neurotransmitter gene expression, in processing any neurotransmitter, in modulating cellular response to any neurotransmitter, or in any other cellular process cannot be determined on the basis of the specification and prior art disclosures. The Examiner stated that the specification teaches at pp. 20-25 that an mRNA encoding SEQ ID NO:6 is associated with the presence of mRNAs encoding one or more neurotransmitter enzymes in cells of paraganglionic tumor tissue, and no more (emphasis added). The Examiner stated that the specification suggests at p. 2 that the polypeptide of SEQ ID NO:6 might be involved in any among a plethora of diseases and disorders of the nervous system, however that while any one of these diseases or disorders is a substantial occurrence, mere allegations of a prospective, potential utility cannot rise to a level of a credible assertion of a specific in vivo utility that is substantial.

The Examiner stated that to address this rejection as it applies to claims 1-6, Applicant is invited to establish a specific utility for a nucleic acid encoding the polypeptide of SEQ ID NO:6 or, alternatively, for the encoded polypeptide, and to show that this utility is substantial. Finally, the Examiner stated that claims 7, 8 and 11 drawn, respectively, to pharmaceutical compositions comprising the encoding nucleic acid or the encoded protein, and to a method of treating no particular disease comprising administering said composition all present the further issue of a credible application.

Applicants respectfully traverse the rejection and submit that the Examiner has not met his burden of proof to provide specific evidence or sound scientific reasoning why one skilled in the art would have reason to doubt Applicants assertion of utility. The Examiner is reminded that the utility requirement, according to established law, is not an onerous one.

To meet the utility requirement of sections 101 and 112 of the Patent Act, the patent applicant need only show that the claimed invention is "practically useful," *Anderson v. Natta*, 480 F.2d 1392, 1397, 178 USPQ 458 (CCPA 1973) and confers a "specific benefit" on the public. *Brenner v. Manson*, 383 U.S. 519, 534-35, 148 USPQ 689 (1966). As discussed in a recent Court of Appeals for the Federal Circuit case, this threshold is not high:

> An invention is "useful" under section 101 if it is capable of providing some identifiable benefit. See *Brenner v. Manson*, 383 U.S. 519, 534 [148 USPQ 689] (1966); *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 [24 USPQ2d 1401] (Fed. Cir. 1992) ("to violate Section 101 the claimed device must be totally incapable of achieving a useful result"); *Fuller v. Berger*, 120 F. 274, 275 (7th Cir. 1903) (test for utility is whether invention "is incapable of serving any beneficial end").

Juicy Whip Inc. v. Orange Bang Inc., 51 USPQ2d 1700 (Fed. Cir. 1999).

While an asserted utility must be described with specificity, the patent applicant need not demonstrate utility to a certainty. In *Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 USPQ2d 1094 (Fed. Cir. 1991), the United States Court of Appeals for the Federal Circuit explained:

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding lack of utility." *Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 762, 221 USPQ 473, 480 (Fed. Cir. 1984).

The specificity requirement is not, therefore, an onerous one. If the asserted utility is described so that a person of ordinary skill in the art would understand how to use the claimed invention, it is sufficiently specific. *See Standard Oil Co. v. Montedison, S.p.a.*, 212 U.S.P.Q. 327, 343 (3d Cir. 1981). The specificity requirement is met unless the asserted utility amounts to a "nebulous expression" such as "biological activity" or "biological properties" that does not convey meaningful information about the utility of what is being claimed. *Cross* v. *Iizuka*, 753 F.2d 1040, 1048 (Fed. Cir. 1985).

In addition to conferring a specific benefit on the public, the benefit must also be "substantial." *Brenner*, 383 U.S. at 534. A "substantial" utility is a practical, "real-world" utility. *Nelson v. Bowler*, 626 F.2d 853, 856, 206 USPQ 881 (CCPA 1980).

If persons of ordinary skill in the art would understand that there is a "well-established" utility for the claimed invention, the threshold is met automatically and the applicant need not make any showing to demonstrate utility. Manual of Patent Examination Procedure at § 706.03(a). Only if there is no "well-established" utility for the claimed invention must the applicant demonstrate the practical benefits of the invention. *Id.*

Once the patent applicant identifies a specific utility, the claimed invention is presumed to possess it. *In re Cortright*, 165 F.3d 1353, 1357, 49 USPQ2d 1464 (Fed. Cir. 1999); *In re Brana*, 51 F.3d 1560, 1566; 34 USPQ2d 1436 (Fed. Cir. 1995). In that case, the Patent Office bears the burden of demonstrating that a person of ordinary skill in the art would reasonably doubt that the asserted utility could be achieved by the claimed invention. *Id.* To do so, the Patent Office must provide evidence or sound scientific reasoning. *See In re Langer*, 503 F.2d 1380, 1391-92, 183 USPQ 288 (CCPA 1974). If and only if the Patent Office makes such a showing, the burden shifts to the applicant to provide rebuttal evidence that would convince the person of ordinary skill that there is sufficient proof of utility. *Brana*, 51 F.3d at 1566. The applicant need only prove a "substantial likelihood" of utility; certainty is not required. *Brenner*, 383 U.S. at 532.

The Examiner's allegation that the specification teaches no more than the mere association of the claimed polynucleotides and their encoded polypeptides with known, and useful neurotransmitter processing genes clearly does not meet the standard of proof discussed above. Likewise, the Examiner's allegation that the association or involvement of the claimed polynucleotides in specific

neurotransmitter related diseases is merely prospective or potential and does not constitute a "substantial likelihood" of utility, does not meet this standard.

In response to the Examiner's invitation to establish a specific utility for a nucleic acid encoding the polypeptide of SEQ ID NO:6, applicants submit that such a utility is disclosed in the specification as filed. Applicants have attached a declaration under 37 CFR 1.132 of Dr. Michael G. Walker, the first inventor on the application and clearly one skilled in the art attesting to the use of the claimed polynucleotide and its encoded protein as surrogate markers for known neurotransmitter processing molecules with which it is coexpressed, and for the diseases and disorders with which the known genes are associated. In his declaration, Dr. Walker first presents independent evidence validating the method of analysis used in the present application to predict coexpression of genes by confirmation of actual expression of genes in predicted tissues (Thompson et al. (2002); Identification and Confirmation of a Module of Coexpressed Genes, Genomics Research 12:1517-1522). The Thompson article further provides evidence of a "substantial likelihood" that such coexpressed genes are also functionally related. The declaration then describes, with reference to the specification and the art of record, the significant coexpression of SEQ ID NO:4 with the specific neurotransmitter processing genes secretogranin I and II, TH, and hVMAT1, and the known association/involvement of these genes in specific neurological disorders, i.e., Parkinson's disease, schizophrenia, and neuroendocrine cancers.

The declaration therefore supports the asserted use of the polynucleotides of the invention as recited in the specification, in the diagnosis and monitoring the progression and treatment of specific neurological disorders associated with neuerotransmitter processing, in particular, the use of SEQ ID NO:4 in the diagnosis and monitoring the progression and treatment of Parkinson's disease, schizophrenia, and neueroendocrine cancers. This utility is achieved without any knowledge of the specific function or biological activity of the encoded protein, although, as noted above, the Thompson article provides independent evidence that such tightly coexpressed genes are likely functionally related.

With respect to the Examiner's allegation that pharmaceutical compositions comprising the claimed polynucleotide or its encoded polypeptide lack a credible use in treating unspecified diseases or conditions, applicants do not acquiesce to the Examiner's contention that the specification does not provide a credible link between the claimed polynucleotides and polypeptide, and specific diseases or

disorders. The specification discloses that all of the known genes found to be coexpressed with SEQ ID NO:4 function in the regulation of catecholamine production and expression and therefore in diseases and disorders associated with dysfunction of this regulation. The specification (and the Thompson article) further supports a substantially likelihood that highly coexpressed genes are likely to be functionally related and to be similarly involved in these processes and associated diseases or disorders. However, in the interests of expediting prosecution and the allowance of claims, applicants have amended claims 7 and 8 to delete the term "pharmaceutical" from the phrase "pharmaceutical composition" canceled claim 11. Compositions comprising polynucleotides or polypeptides and biocompatible pharmaceutical carriers, such as saline, buffered saline, dextrose, and water, specifically disclosed in the specification at p. 16, lines 23-24, are well known in the art to be useful for providing stable compositions for biological materials for storage and transport.

With these arguments and amendments, applicants submit that the claimed invention, at least as recited in claims 2 and 4-8 are supported by a specific and substantial utility that is also credible, and therefore request withdrawal of the rejection of these claims under 35 U.S.C. § 101.

35 U.S.C. § 112, First Paragraph, Rejection of Claims 1-8 and 11

The Examiner has rejected claims 1-8 and 11 under 35 U.S.C. § 112, first paragraph, specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art would clearly not no how to use the claimed invention.

To the extent that this rejection is based on the unsupported grounds of the rejection of these claims under 35 U.S.C. § 101 for the reasons given above, applicants likewise request withdrawal of the rejection of these claims under 35 U.S.C. § 112, first paragraph.

35 U.S.C. § 112, First Paragraph, Rejection of Claims 7, 8 and 11

The Examiner has rejected claims 7, 8, and 11 under 35 U.S.C. § 112, first paragraph, as containing subject matter which is not described in the specification in such a was as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, the Examiner stated that the specification fails to exemplify or describe the preparation of the subject matters of claims 7, 8 and 11. The Examiner

stated that where the specification fails to identify, exemplify, describe, or even suggest the biological role of the polypeptide of SEQ ID NO:6 or a nucleic acid encoding it, it cannot describe the preparation (of) pharmaceutical compositions comprising these compounds. The specification's treatment of the claimed subject matter is considered to be entirely prospective where skilled artisans in the relevant field of molecular biology could not predict the biological roles of the products comprised by the claimed pharmaceutical compositions or methods thereof.

The amendments to claims 7 and 8 have been discussed above, and claim 11 has been canceled. Applicants again do not do not acquiesce to the Examiner's contention that the specification does not provide a credible link between the claimed polynucleotides and polypeptide an specific diseases or disorders for the reasons given previously. However, applicants submit that the inventor(s) were clearly in possession of the claimed invention, as recited in amended claims 7 and 8 and therefore request withdrawal of the rejection of these claims under 35 U.S.C. § 112, first paragraph.

35 U.S.C. § 112, First Paragraph, Rejection of Claims 7, 8 and 11

The Examiner has rejected claims 7, 8 and 11 under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for designing a nucleic acid sequence encoding the polypeptide of SEQ ID NO:6, and for preparing the encoded polypeptide, does not reasonably provide enablement for preparing a pharmaceutical composition comprising either product nor enablement for a method of use of such a pharmaceutical composition in treating any disease or medical condition. The Examiner stated that claims 7, 8 and 11 contemplate arbitrary formulation of pharmaceutical compositions where there is no description or suggestion of any target cells or tissues, nor any description or suggestion of a specific disease or medical condition that such compositions might have an effect on. Indeed, the Examiner stated, neither the prior art made of record herewith nor Applicant's specification can identify, taken together, the biological function of compounds of either composition.

Applicants again reiterate the amendments to claims 7 and 8 and the cancellation of claim 11. Amended claims 7 and 8 are fully enabled by the specification and that which is well known in the art, for the reasons given above in the response to the rejection of these claims under 35 U.S.C. §§ 101/112, and therefore request withdrawal of the rejection of these claims under 35 U.S.C. § 112, first paragraph for lack of enablement.

35 U.S.C. § 102(b), Rejection of Claim1

Claim 1 stands rejected under 35 U.S.C. § 102(b) as being anticipated by Schalling et al. (European Neuropsychopharmacology, 1991, Vol. 1, pp. 173-176) or in the alternative, Wessel et al. (Molecular Brain Research, 1992, Vol. 15, pp. 349-360). The Examiner stated that Schalling et al. disclose coexpression of genes that encode phenylethanolamine N-methyltransferase (PNMT) and tyrosine hydroxylase (TH), the latter gene recited in claim 1. Similarly, Wessel et al disclose the coexpression of genes encoding both TH and dopamine-beta-hydroxylase (DBH), which genes are recited in claim 1 together with PNMT. The Examiner stated that since a PNMT-encoding cDNA had previously been isolated in order to prepare the hybridization probe used either by Schalling et al. or Wesser et al., their disclosure inherently anticipates the subject matter of claim 1. Claim 1 has been canceled, and Applicants therefore request withdrawal of the rejection of claim 1 under 35 U.S.C. § 102(b) as being anticipated by Schalling et al. or Wessel et al.

35 U.S.C. § 102 (b), Rejection of Claims 1 and 3

Claims 1 and 3 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Yamada et al. (Histochemistry, 1992, Vol 97, pp. 201-206) or in the alternative, by Zellmer et al. (The Journal of Neuroscience, 1995, Vol. 15, pp. 8109-8120). The Examiner stated that Yamada et al. disclose the coexpression of genes encoding TH and PNMT and further disclose the presence of both the PNMT and TH polypeptide products, thus anticipating the subject mater of both claims 1 and 3. Similarly, Zellmer et al. disclose the isolation of a polynucleotide encoding the homeobox protein Arix expressed together with the DBH gene, anticipating the subject mater of claim 1, and also disclose the encoded amino acid sequence of Arix, thus anticipating the subject matter of claim 3. Claims 1 and 3 have been canceled, and Applicants therefore request withdrawal of the rejection of claims 1 and 3 under 35 U.S.C. § 102(b) as being anticipated by Yamada et al. or Zellmer et al.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited. Applicants further request that upon allowance of claim 2, that claim 10 be rejoined and examined as a process claim that depends from and is of the same scope as product claim 2 in accordance with MPEP § 821.04 and *in re* Ochiai.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Agent of Record, below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 1, 3 and 11 have been canceled.

Claims 2, 4, 7, and 8 have been amended as follows:

2. (Once Amended) A substantially purified [The] polynucleotide [of claim 1], comprising a polynucleotide sequence selected from:

(a) a polynucleotide sequence selected from the group consisting of SEQ ID NOs: 1-5;

(b) a polynucleotide sequence which encodes the polypeptide sequence of SEQ ID NO: 6;

(c) a polynucleotide sequence which is completely complementary to the polynucleotide sequence of (a) or (b); and

(d) A naturally-occurring variant of [a probe which hybridizes to] the polynucleotide of (a), (b), or (c), having at least 95% identity to the polynucleotide sequence of (a), (b), or (c).

4. (Once Amended) A substantially purified [The] polypeptide [of claim 3], comprising a polypeptide sequence selected from:

(a) the polypeptide sequence of SEQ ID NO: 6;

(b) a polypeptide sequence comprising at least 6 sequential amino acids of the polypeptide sequence of (a); and

(c) a variant of the polypeptide sequence of SEQ ID NO:6 having at least 95% identity to the polypeptide sequence of SEQ ID NO:6.

7. (Once Amended) A [pharmaceutical] composition comprising the polynucleotide of claim 2 in conjunction with a suitable pharmaceutical carrier.

8. (Once Amended) A [pharmaceutical] composition comprising the polypeptide of claim 4 in conjunction with a suitable pharmaceutical carrier.